

REVIEW

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Prevalence, incidence and risk factors for anogenital warts in Sub Saharan Africa: a systematic review and meta analysis

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Abstract

Introduction: The quadrivalent HPV vaccine is highly effective in primary prevention of anogenital warts (AGWs). However, there is lack of systematic review in the literature of the epidemiology of AGWs in Sub Saharan Africa (SSA).

Objective: To review the prevalence, incidence and risk factors for AGWs in SSA prior to the introduction of HPV vaccination programs.

Methods: PubMed/MEDLINE, Africa Index Medicus and HINARI websites were searched for peer reviewed English language published medical literature on AGWs from January 1, 1984 to June 30, 2012. Relevant additional references cited in published papers were also evaluated for inclusion. For inclusion, the article had to meet the following criteria (1) original studies with estimated prevalence and/or incidence rates among men and/or women (2) detailed description of the study population (3) clinical or self-reported diagnosis of AGWs (4) HPV genotyping of histologically confirmed AGWs. The final analysis included 40 studies. Data across different studies were synthesized using descriptive statistics for various subgroups of females and males by geographical area. A meta - analysis of relative risk was conducted for studies that had data reported by HIV status.

Results: The prevalence rates of clinical AGWs among sex workers and women with sexually transmitted diseases (STDs) or at high risk of sexually transmitted infection (STIs) range from 3.3% - 10.7% in East, 2.4% - 14.0% in Central and South, and 3.5% - 10.5% in West African regions. Among pregnant women, the prevalence rates range from 0.4% - 3.0% in East, 0.2% - 7.3% in Central and South and 2.9% in West African regions. Among men, the prevalence rates range from 3.5% - 4.5% in East, 4.8% - 6.0% in Central and South and 4.1% to 7.0% in West African regions. In all regions, the prevalence rates were significantly higher among HIV+ than HIV- women with an overall summary relative risk of 1.62 (95% CI: 1.43-1.82). The incidence rates range from 1.1 - 2.7 per 100 person-years among women and 1.4 per 100 person years among men. Incidence rate was higher among HIV+ (3.0 per 100 person years) and uncircumcised men (1.7 per 100 person-years) than circumcised men (1.3 per 100 person-years).

HIV positivity was a risk factor for AGWs among both men and women. Other risk factors in women include presence of abnormal cervical cytology, co-infection with HPV 52, concurrent bacteria vaginoses and genital ulceration. Among men, other risk factors include cigarette smoking and lack of circumcision.

Conclusions: AGWs are common among selected populations particularly HIV infected men and women. However, there is need for population-based studies that will guide policies on effective prevention, treatment and control of AGWs.

Keywords: Anogenital warts, Sub Saharan Africa, HIV, HPV vaccination

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Introduction

The epidemiology of AGWs in most of SSA is largely unknown since few studies have been conducted. Studies from high income countries show that the clinical burden has been increasing over the years since approximately 0.5-1.0% of adults below 50 years have AGWs [1-3].

Caused mainly by low-risk HPV type 6 and 11, AGWs affect both men and women [1]. They are highly infectious with about 65% of individuals with an infected partner developing lesions within 3 weeks [4]. The median time between infection and development of lesions is about 11–12 months among men [5,6] and about 5–6 months among women [7]. Rarely, AGWs have been associated with malignant Bushke-Lowenstein malignant tumors [8]. Their occurrence is strongly linked to HIV and weakly associated with cigarette smoking [1,4,5]. At present, the impact of highly active anti-retroviral therapy (HAART) remains unclear [5,6].

Except for Rwanda [9], most countries in SSA are yet to introduce or scale up HPV vaccination in national immunization programs. While reduction in disease burden due to HPV 16/18 may not be evident for decades, vaccination with the quadrivalent HPV vaccine should result in immediate measurable reduction in the incidence rate of AGWs. Preliminary results from the Australian national HPV vaccination program shows a significant decline in the number of cases of AGWs among the young vaccinated women and some herd-immunity effect in young unvaccinated heterosexual men [10]. This review was undertaken to assess the prevalence, incidence and risk factors for AGWs before the introduction of HPV vaccination programs in order to provide a basis for future program evaluation in SSA.

Methods

Identification and eligibility of relevant studies

PubMed/MEDLINE, Africa Index Medicus and HINARI websites were searched for peer reviewed English language published medical literature from January 1, 1984 up to June 30, 2012. The following Medical Subject Heading (MESH) and search terms were used alone or in combination “Sub Saharan Africa” AND (“anogenital warts” OR “venereal warts” OR “condylomata acuminata” OR “condylomata”) AND “risk factors”. Relevant additional references cited in published papers were also evaluated for inclusion. For inclusion, articles had to meet the following criteria (1) original studies with clear estimation of prevalence and/or incidence rates among men and/or women (2) detailed description of study population (3) clinical or self-reported diagnosis of AGWs (4) HPV genotyping of histologically confirmed AGWs. Studies focusing exclusively on case reports and commentaries were excluded.

Data extraction

From each article, the following information was extracted: first author, publication journal name and year of publication, country of study population, study sample type (population- or clinic- based), study design, mean or median age with range/inter quartile range, whenever available, sample size, prevalence and/or incidence rate overall and by HIV status, whenever available, risk factors and the overall prevalence of HIV, whenever available. For studies that included populations from different countries, data was extracted separately for each country.

Statistical analysis

Data across different studies were synthesized using descriptive statistics for different subgroups of females and males by geographical areas. A meta-analysis of relative risk was conducted for studies that had data reported by HIV status and results presented in a forest plot. In total, 40 studies (39 hospital - and 1 population-based) are included in this review.

Results

The prevalence and incidence rates of AGWs in diverse female and male hospital-based study populations in East, Central and South, and West African regions is summarized in Tables 1, 2 and 3. Overall, there is inter- and intra-region variations in rates depending on the underlying prevalence rate of HIV-1 infection, study population and age group studied. While both young and adult populations were studied, there seems to be no trend or pattern of prevalence rates by age.

Prevalence rates among women by geographical region

The prevalence rates among women in East, Central and South, and West African regions are summarized in Tables 1. The prevalence rates of clinical AGWs among sex workers and women with STDs or at high risk for other STIs range from 3.3% - 10.7% in East, 2.4% - 14.0% in Central and South, and 3.5% - 10.5% in West African regions. Among pregnant women, the prevalence rates range from 0.4% - 3.0% in East, 0.2% - 7.3% in Central and South and 2.9% (single study) in West African regions.

Prevalence rates of AGWs among men by geographical region

Eight (8) studies (3 East Africa, 2 Central and South Africa, 3 West Africa) reported prevalence rates of AGWs in men (Table 2). The prevalence rate among STD clinic attendees, men who have sex with men, and men with symptoms of STDs in Central and South and West African region range from 4.8% - 12.2% and 2.8% - 4.1%,

Table 1 Studies reporting prevalence of AGWs in women

Author, Publication year	Country	Study design	Study population	Sample size	Mean or Median age (years, range/IQR ¹)	Prevalence of AGWs ² n (%)	Prevalence of HIV-1 (%)	Comments
East Africa								
Kreiss et al., 1992 [11]	Kenya	⁵ Cross-sectional	Sex workers	196	30.2 (HIV-1+) 31.5 (HIV-1-)	18/196 (9.2) Overall 15/145 (10.0) HIV-1+ 3/51 (6.0) HIV-1		
Fonck, et al., 2000 [12]	Kenya	"EntryTbl_st" ⁵ Cross-sectional	Women attending STD ³ clinic	520	26 ± 6.8 (14–49)	31/520 (6.0) 5/520 (1.0) ^a	29.0	Prevalence of AGWs 5% (Non pregnant women) 9% (Pregnant women) 6% (One sexual partner)
Mayaud et al., 2001 [13]	Tanzania	⁵ Cross-sectional	Pregnant women	660	23.4 ± 5.1 (15–44)	20/660 (3.0)	15.0	
Riedner et al., 2003 [14]	Tanzania	⁵ Open cohort	Female bar workers	600	25.4	39/600 (6.5) Overall 39/408 (9.6) HIV + 0/192 (0.0) HIV -	68.0	
Namkinga et al., 2005 [15]	Tanzania	⁵ Cross-sectional	Women presenting with complaints of genital infections	464		18/464 (3.9)	22.0	
Amone-P'Olak, 2005 [16]	Uganda	⁴ Cross-sectional	Formally abducted teenage girls in Northern Uganda	123	16.2 ± 2.2 (12–18)	67/123 (54.5) ^a		
Mbizvo et al., 2005 [17]	Tanzania	⁵ Cross-sectional	Women seeking primary health care services	382	26.7 ± 6.0	8/382 (2.1)	11.5	
Msuya et al., 2006 [18]	Tanzania	⁵ Cross-sectional	Women seeking reproductive health care services	382	24.6 (14–43)	7/382 (2.0)	6.9	
Riedner et al., 2006 [19]	Tanzania	⁵ Serial cross-sectional	Female bar workers	600	25.5 (16–39)	5.2-10.7	67.0	
Aboud et al., 2008 [20]	TanzaniaMalawi and Zambia	⁵ Cross-sectional	HIV-1 positive pregnant women	2292	(15–49)	195/2292 (8.5)		Prevalence of AGWs Blantyre – 42/474 (8.9) Lilongwe – 61/748 (8.2) Dar es Salaam – 31/428 (7.2) Lusaka – 61/642 (9.5)
Banura et al., 2008a [21]	Uganda	Baseline of a prospective cohort study	Young women attending a clinic for teenagers	1275	20 (12–24)	97/1275 (7.6)	8.6	
Banura et al., 2008b [22]	Uganda	⁵ Baseline of a prospective cohort study	Pregnant women Attending ANC ⁵	987	19 (14–24)	61/987 (6.2)	7.3	
Urassa et al., 2008 [23]	Tanzania	⁵ Cross-sectional	Youth attending an STI ⁴ clinic	214	20.2 (Females) (13–24) 21.5 (Males) (11–24)	7/214 (3.3)	15.3	HIV –1 prevalence in Males – 7.5%
Grijssen et al., 2008 [24]	Kenya	⁵ Baseline of a prospective cohort study	Women at risk for HIV-infection	361	27 (23–32)	8/361 (2.4)	32.0	
Msuya et al., 2009 [18]	Tanzania	⁵ Cross-sectional	Pregnant women	2655	24.6 (14–43)	11/2555 (0.4) Overall 2/184 (1.1) HIV + 9/2470 (0.4) HIV -	6.9	

Table 1 Studies reporting prevalence of AGWs in women (Continued)

Mapingure, et al., 2000 [25]	Tanzania	⁵ Cross-sectional	Pregnant women	2654	24.6	34/2654 (1.3) 48/2654 (1.8) ^b	6.9		
Central and South Africa									
Latif et al., 1984 [26]	Zimbabwe	⁵ Cross-sectional	Pregnant women attending STD clinic	175	22.3	23/175 (13.7)			
Mason et al., 1990 [27]	Zimbabwe	⁵ Cross-sectional	Women attending STD clinic	100	(15–45)	14/100 (14.0) 1/59 (1.7) ^a			
Kristensen 1990 [28]	Malawi	⁵ Cross sectional	Adult women with symptoms of STIs	16,218	26.8 ± 7.5	32/16,218 (0.2)	62.4		
Nzila et al., 1991 [29]	Democratic Republic of Congo	⁵ Cross-sectional	Female sex workers	1233		30/1233 (2.4) Overall 21/431 (5.0) HIV + 8/802 (1.0) HIV-	35.0		
Le Bacq et al., 1993 [30]	Zimbabwe	⁵ Cross-sectional	New STD clinic attendees	146		19/146 (13.0)	69.0		
Maher et al., 1995 [31]	Malawi	⁵ Cross-sectional	Female patients in general medical care	61	31 (16–65)	6/61 (9.8)			
Taha et al., 1998 [32]	Malawi	⁵ Serial cross-sectional surveys	Pregnant women	1990 – 6603 HIV + 1502 HIV- 5101 1993 – 2161 HIV + 694 HIV- 1457 1995 – 808 HIV + 808 HIV- 701		1990 1993 1995 Overall 4.8 3.1 2.5 HIV + 8.3 6.3 2.7 HIV- 2.2 1.7 1.0	23.0 (1990) 30.1 (1993) 32.6 (1995)		
Claskala et al., 2005 [33]	Zambia	⁵ Cross-sectional	Pregnant women	3160	25 ± 5.3 (14–43)	203/3160 (6.2)			
Mbizvo et al., 2005 [17]	Zimbabwe	⁵ Cross-sectional	Women recruited from primary health care centers	386	26.5 ± 6.8	13/386 (3.4)	29.3		
Kurewa et al., 2010 [34]	Zimbabwe	⁵ Cross-sectional	Pregnant women	691	24.2 ± 5.1	48/691 (7.0) 50 /691 (7.3) ^a	25.6		
Mapingure et al., 2010 [26]	Zimbabwe	⁵ Cross-sectional	Pregnant women	691	24.2 ± 5.1	50/691 (7.3) 33/691 (4.8) ^b	25.6		
Menendez et al., 2010 [35]	Mozambique	⁵ Cross-sectional	Women attending ANC and FP ⁵ clinics and community	262	(14–61)	13/262 (5.0)	12.0	Prevalence of HIV-1 21.0% among FP clinic attendees	
West Africa									
Oni et al., 1994 [36]	Nigeria	⁵ Cross-sectional	STD clinic attendees	116		12/116 (10.5)			
Ghys et al., 1995 [37]	Ivory Cost	⁵ Cross sectional	Female sexual workers	1209		105/1209 (8.7) Overall 79/567 (14.0) HIV + 26/642 (4.0) HIV -	80.0		
Meda et al., 1997 [38]	Burkina Faso	⁵ Cross-sectional	Women attending ANC	645	25.3 ± 2.9 (15–41)	19/645 (2.9)			
Okesola et al., 2000 [39]	Nigeria	⁵ Cross-sectional	Patients attending an STD clinic	861	(17–74)	68/861 (8.0)			

Table 1 Studies reporting prevalence of AGWs in women (Continued)

Bakare et al., 2002 [40]	Nigeria	⁵ Cross-sectional	CSWs ⁷ and women without symptoms of STIs			6.5 36.4 ^c	34.3	
Domfeh et al., 2008 [41]	Ghana	⁵ Cross-sectional	Women attending gynecological clinic	75		33.3 ± 9.2 (19–57)	4/75 (5.3) ^a	
Sagay et al., 2009 [42]	Nigeria	⁵ Cross-sectional	Female sex workers	374		27.8 ± 6.7 (16–63)	17/374 (4.5)	Prevalence of AGWs 5/81 (6.1%) Lemon users 12/293 (4.1%) Non Lemon users
Jombo et al., 2009 [43]	Nigeria	⁵ Cross-sectional	Patients with genital ulcer disease	699			369/699 (52.8) Overall 285/506 (56.4) HIV + 84/193 (43.6) HIV –	Prevalence <i>Males</i> : 13/329 (2.6%) <i>Females</i> : 8/177 (1.6%)
Low et al., 2011 [44]	Burkina Faso	⁵ Baseline of Prospective cohort	CSWs and other women with high-risk sexual behaviors	765		28 (15–54)	27/765 (3.5) Overall 19/273 (7.0) HIV –1 + 8/492 (1.6) HIV –	34.9 HIV-1 0.7 HIV-1 & 2 No prevalent AGWs among women on HAART

^a self-reported prevalence; ^b self-reported prevalence for the last 12 months; ^c self-reported prevalence among commercial sexual workers; ¹ Inter quartile range; ² Anogenital warts; ³ Sexually transmitted disease; ⁴ Sexually transmitted infection; ⁵ Antenatal care; ⁶ Family planning; ⁷ Commercial sexual workers; ⁸ hospital-based study; [†] Teenagers in an institution.

Table 2 Studies reporting AGWs in men

Author, year	Country	Study design	Study population	Sample size	Mean or Median age (years, range/IQR ¹)	Prevalence of AGWs ² (%)	Prevalence of HIV-1%	Comments
East Africa								
Grijzen et al., 2008 [24]	Kenya	⁵ Baseline of a prospective cohort study	Men at high-risk for HIV infection	536	27 (24–33)	9/500 (1.8)	21.0	
Smith et al., 2010 [45]	Kenya	⁵ Baseline of RCT ³ on male circumcision	HIV negative sexually active men	2168	20 (19–28)	12/2168 (0.6) Overall 10/1089 (0.9) HIV + 2/1079 (0.2) HIV-		
Tobian et al., 2012 [46]	Uganda	¹ Cross-sectional	Heterosexual men	1399	15-49	23/1399 (1.6) ³ Overall 16/421 (3.8) ^a HIV + 7/978 (0.7) ^a HIV –		
Central and South Africa								
Le Bacq et al., 1993 [31]	Zimbabwe	⁵ Cross-sectional	New STD clinic attendees	319		39/319 (12.2)	61.0	
Maher et al. 1995 [32]	Malawi	⁵ Cross-sectional	In-patient male patients in general medical care	62	39 (20–90)	3/62 (4.8)		
Machekano et al., 2000 [47]	Zimbabwe	⁵ Baseline of prospective cohort study	Male factory workers who reported symptoms of STDs	374		22/374 (6.0)	20	
Müller et al., 2010 [48]	South Africa	⁵ Cross-sectional	Heterosexual men attending sexual health services	214	29.8 ± 7.5	108/214 (50.5)	49.5	
West Africa								
Okesola et al., 2000 [40]	Nigeria	⁵ Cross-sectional	STD ² clinic attendees	1,373	17-74	4.1		
Wade et al., 2005 [49]	Senegal	⁵ Cross sectional	Men who have sex with men	463	18-52	13/463 (2.8)	18.1	21.5% Overall 0.5% HIV-2 2.9% HIV-1 & HIV-

^a Self-reported prevalence.

¹ Inter Quartile Range.

² Commercial sexual workers.

³ Randomized Controlled Trial.

⁵ hospital-based study.

¹ Population-based study.

Table 3 Studies reporting incidence rates of AGWs in men and women

Author, year	Country	Study design	Study population and site	Sample size	Mean or median age (years, range)	Incidence rate/100 person-years of AGWs ²	HIV -1 prevalence%	Comments
East Africa								
Lavreys et al., 1999 [50]	Kenya	Prospective cohort	HIV negative truck drivers in Mombasa	746	26 ^a (17–58) 29 ^b (16–62)	1.4 overall 1.7 Uncircumcised 1.3 Circumcised		Annual incidence of HIV-1 – 3.0%
West Africa								
Ozumba et al., 1991 [51]	Nigeria	Retrospective cohort (1976–85)	Female STD ¹ clinic attendees	45	21 (5–36)	2.7 (range:1.6 – 3.6)		AGWs incidence highest among teenagers and students
Low et al., 2011 [44]	Burkina Faso	Prospective cohort	Female sex workers and other women at high risk	765	28 (15–54)	1.1 HIV -	34.9	HIV- 1 & HIV-2 prevalence 0.7%

^a uncircumcised men.

^b circumcised men.

¹Sexually Transmitted Diseases.

²Anogenital warts.

respectively. The rates among men in the East African region range from 0.6 -1.8 percent.

Prevalence rates by HIV status

The prevalence rates of AGWs were significantly higher among HIV+ than HIV- women in all regions with an overall summary relative risk of 1.62 (95% CI: 1.43–1.82) (Figure 1). Similarly among men, clinical and self -reported

prevalence rates were higher among HIV+ than HIV- men (Table 2).

Incidence rates of AGWs among men and women

Only 3 studies (2 among females and 1 among males) reported incidence rates of AGWs (Table 3). The incidence rates range from 1.1 – 2.7 per 100 person-years among women and 1.4 per 100 person years among

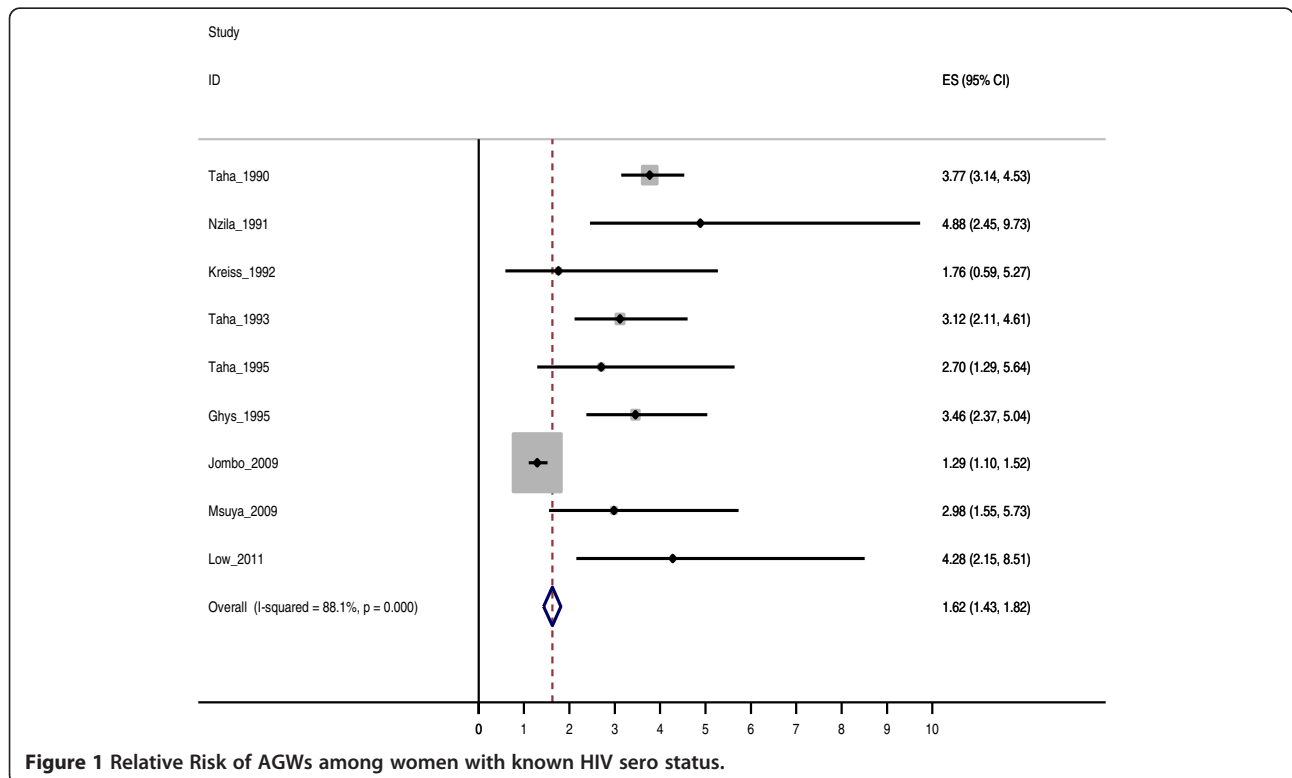


Figure 1 Relative Risk of AGWs among women with known HIV sero status.

men. The incidence rate was higher among uncircumcised (1.7 per 100 person-years) than circumcised men (1.3 per 100 person-years) [44].

HPV 6 and/or 11 in AGWs

Only 3 studies reported the prevalence of HPV 6 and/or 11 in biopsy specimens or swabs taken from AGWs. HPV 11 was detected in 100% vulval-vaginal wart specimens obtained from 9 prepubescent South African girls [52]. HPV 6 and/or 11 was detected in 96.3% of 108 genital swabs taken from heterosexual men with AGWs attending sexual health clinics in South Africa [48]. Among 74 specimens taken from penile warts of HIV+ men in South Africa, HPV 6 was detected in 42.5%, HPV 11 in 32.9% and HPV 6/11 in 68.5% [53].

Risk factors for AGWs

Only 2 studies (one among women and another among men) reported on risk factors for AGWs. Among women, the risk of prevalent AGWs was 5 times higher among HIV-1+ than HIV-1- women and 3 times higher among women who smoked cigarettes than those who did not. Among HIV-1+ women with low CD4+ count (≤ 200 cells/ μ L), the risk of incident AGWs was elevated 20 fold, and 6fold for women with CD4+ count >200 cells/ μ L. Other risk factors for incident AGWs in women include detection of HPV 6, concurrent bacterial vaginoses, genital ulceration, presence of abnormal cervical cytology and the detection of cervical HPV 52 [44]. Lack of circumcision and HIV infection were risk factors for AGWs in men [45].

Discussion

To the best of our knowledge this is the first systematic review of the epidemiology of AGWs in SSA. The literature suggests that AGWs are prevalent among both men and women populations seeking care in their respective health care systems. The fewer studies among men is not surprising given that women generally have more frequent contact with the health care system than men. Although there is no marked difference between regions, absence of a standardized protocol for diagnosis might have contributed to the observed variations across studies within the same region. Overall, the prevalence rates were higher than those reported from retrospective administrative databases or medical chart reviews in high income countries possibly because of underlying HIV infection in several studies [54].

Consistent with published studies, the risk for AGWs was higher for HIV+ than HIV- men and women [55]. HIV+ women had almost 2 fold risk for HPV infection than HIV-women. While some AGWs may have been a result of new infections, recrudescence of existing HPV infection has been reported among sexually inactive HIV+ women [56].

Impaired CD4+ T-lymphocyte response and other forms of immune dysfunction may be responsible for altering the natural history of HPV infection among HIV infected individuals [57]. The use of highly active anti-retroviral therapy has been shown to reduce the risk of opportunistic malignancies such as Kaposi sarcoma among HIV+ individuals [58], however, their impact on AGWs remains unclear [55,57,59]. On the other hand consistent use of male condoms appears to reduce the risk by 60-70% [60].

Consistent with other studies, HPV 6 and 11 alone or in combination were detected in the few studies that examined HPV genotypes in AGWs specimens albeit small sample sizes. However, the contribution of HPV 11 to the development of AGWs remains unclear [4,7]. The concurrent detection of HPV 52 with HPV 6 was not surprising as co-infection with high risk HPV types has been reported in 20-50% of AGWs [61,62].

In the absence of a clinical test to establish sub clinical HPV 6 and 11 infections, identification of risk factors for acquisition of AGWs independent of other STDs is complex. Consistent with other studies, low CD4+ cell count (≤ 200 cells/ μ L) and abnormal cervical and anal dysplasias are risk factors for AGWs in HIV+ women and men, respectively [63,64]. Other risk factors for AGWs in women identified in this review included co-infection with HPV 52, and concurrent bacteria vaginoses [65]. In men, anal HPV infection and related dysplasias [39] and lack of circumcision [45] were additional risk factors.

Although AGWs are not life threatening, they cause significant psychological distress and are refractory to conventional therapies, hence the need for prevention [4,66]. The quadrivalent HPV vaccine, correct and consistent condom use and limiting the number of sexual partners are some of the prevention options available to reduce the risk of contracting AGWs.

It is important to note that there are limitations to this study. This review focused only on peer reviewed English language articles published from a few SSA countries, which limits generalization of the findings. Secondly, most studies were conducted in hospital-based study populations, which would favor higher rates than in the general population. Thirdly, the rates should be interpreted with caution because of the differences in study populations and age group studied. While some studies included all adults [31,39], others focused on narrow age ranges of specific populations like young people and pregnant women [23,25] that could have resulted in the observed high rates. Nevertheless, the review provides vital baseline data against which the impact of HPV vaccination could be evaluated in future.

Conclusions

AGWs are common among selected populations particularly HIV+ men and women. However, there is need

for population-based studies on AGWs that will guide policies on effective prevention, treatment and control services.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CB conceived the study, searched the literature, drafted the manuscript and produced the final tables FMM, JO, AKB, SK, EKM made substantial contributions to the manuscript and contributed to data interpretation. All authors read and approved the final manuscript.

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